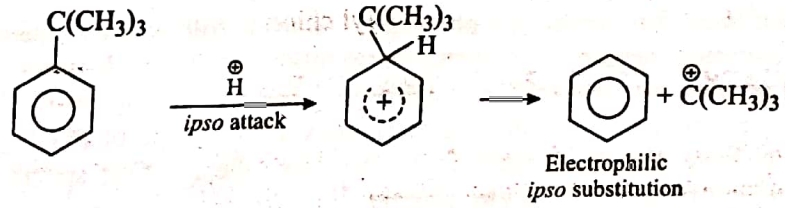
M.Sc. II Semester
Sub - Chemistry
Paper - II (Organic Chemistry)

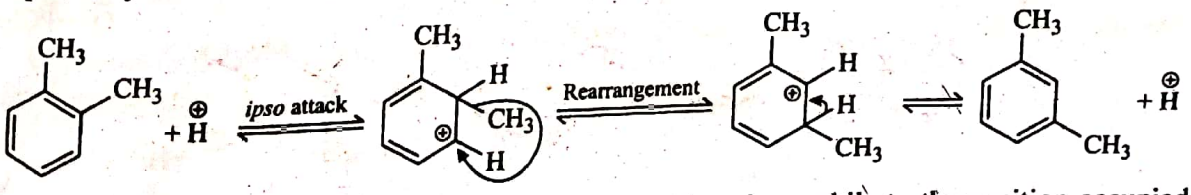
6.10 *IPSO* ATTACK

A position which is already occupied by a non-hydrogen substituent in an aromatic ring is called *ipso* position (Latin : *ipso*, on itself), the attack on this position is called *ipso* attack (or *ipso* addition), and the aromatic substitution in which a substituent already present is replaced is called *ipso* substitution. For example, protodealkylation of an alkylbenzene (reverse of Friedel-Crafts alkylation). In this reaction tertiary alkyl groups are most easily removed, since they depart as stabler carbocations. Thus, *t*-butyl group is used to protect the most reactive position in a compound to effect reaction elsewhere. The mechanism is as follows :



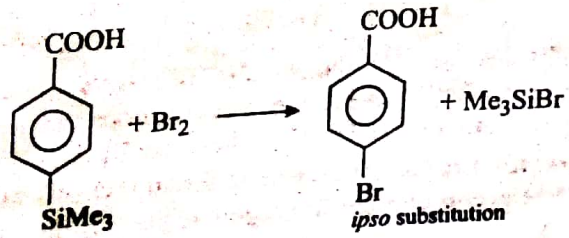
$$(CH_3)_3\overset{\oplus}{C} \longrightarrow (CH_3)_2C{=}CH_2 + H^{\oplus}$$

The rearrangement of alkylbenzenes leading to their isomerisation also involves *ipso* attack. For example, *o*-xylene isomerises to *m*-xylene as follows :



Silyl group has a strong tendency to direct the entering electrophile to the position occupied by it, *i.e.*, *ipso* position. This is due to the strong stabilisation of cationic centre β to the silicon.

Bromodesilylation :



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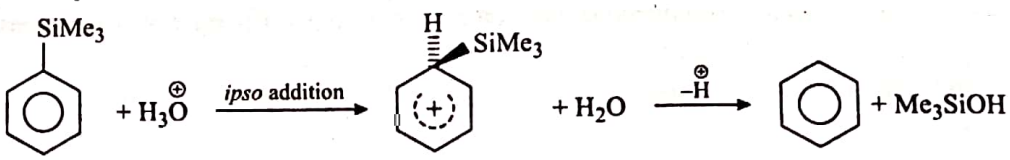
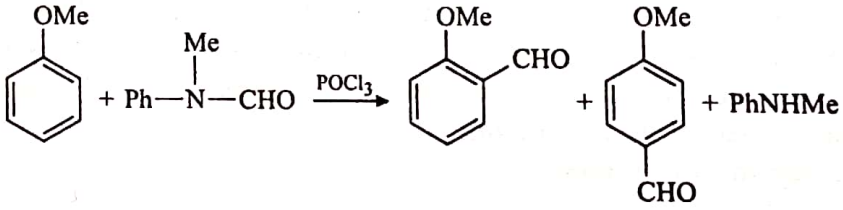
Protodesilylation :



6.11 SOME IMPORTANT NAME REACTIONS INVOLVING AROMATIC ELECTROPHILIC SUBSTITUTION MECHANISM

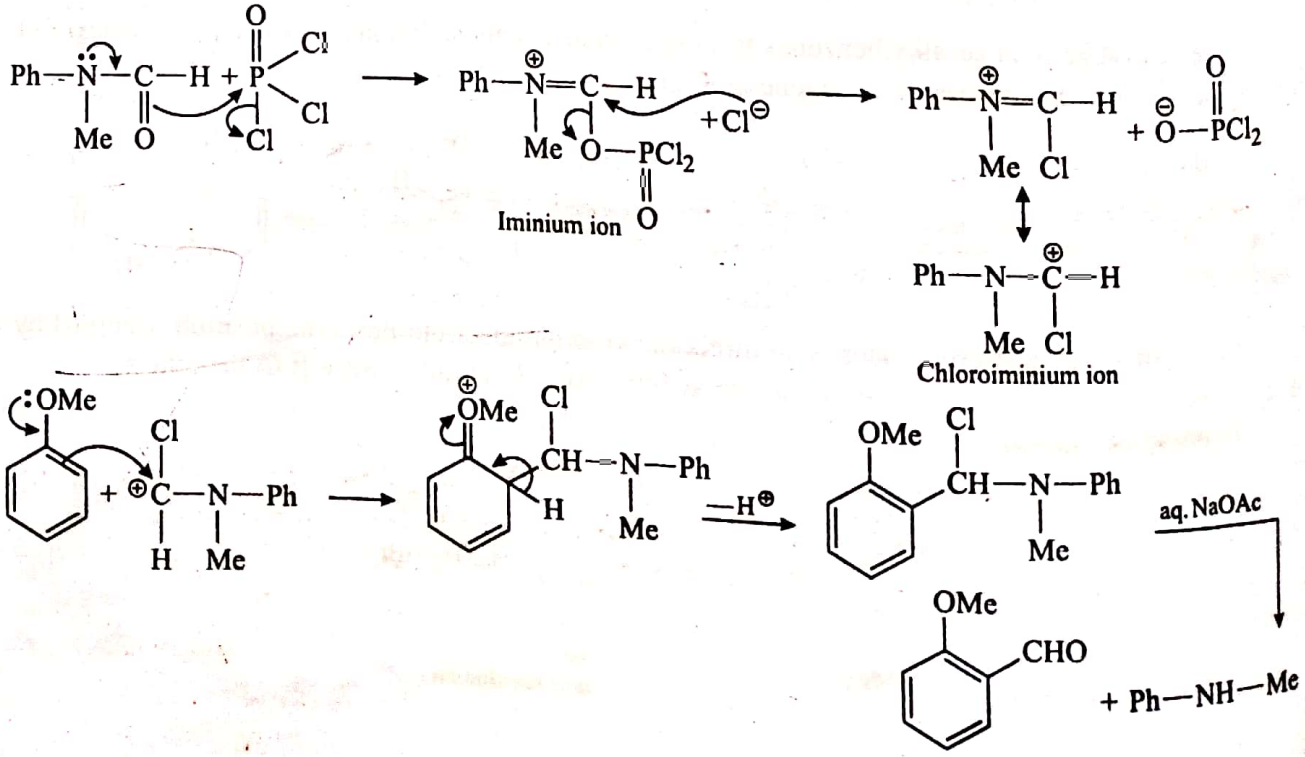
1. Vilsmeier-Haack Reaction

Formylation of active aromatic compounds, like phenolic ethers and dialkylanilines in *o* and *p*-positions, with disubstituted formamide and phosphorus oxychloride is called Vilsmeier or Vilsmeier-Haack reaction. Aromatic hydrocarbons (*e.g.*, azulenes, ferrocenes) and heterocycles, which are more reactive than benzene, can also be formylated. The formylation is carried out by treating the



compound with disubstituted formamide and phosphoryl chloride followed by aqueous sodium acetate. Although the most common reagent is *N*-methylformanilide (*N*-phenyl-*N*-methylformamide), other simple or substituted amides are also used, *e.g.*, DMF, etc. The reaction has also been carried out with disubstituted amides other than formamide to give ketones. In the place of $POCl_3$, other halides such as $SOCl_2$, and $COCl_2$ have also been used. In all the cases the reacting species of the reaction is chloroiminium ion, which behaves as an electrophile.

Mechanism :



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Certain heterocyclic compounds

reaction.

3. Gatterman-Koch Reaction

Certain aromatic compounds can be formylated with a mixture of CO and HCl in the presence of $AlCl_3$. This reaction is known as Gatterman-Koch reaction. The reaction is generally limited to benzene and alkylbenzenes. It does not take place with phenols, phenolic ethers, and rings which contain *meta*-directing substituents. The formylation takes place mostly at the *para* position. Cuprous chloride is necessasry if the reaction is to be carried out at atmospheric pressure. At high pressures (150-200 atm) cuprous chloride is not needed.

$$ArH + CO + HCl \xrightarrow[CuCl]{AlCl_3} ArCHO$$

The mechanism of this reaction is uncertain, but probably the formyl cation ($\overset{\oplus}{HC}{=}O$) is the active electrophilic species. The function of cuprous chloride is to co-ordinate with CO to provide its higher local concentration.

$$CO + HCl + AlCl_3 \longrightarrow [\overset{\oplus}{HC}{=}O \longleftrightarrow HC{\equiv}\overset{\oplus}{O}]\ \overset{\oplus}{AlCl_4}$$

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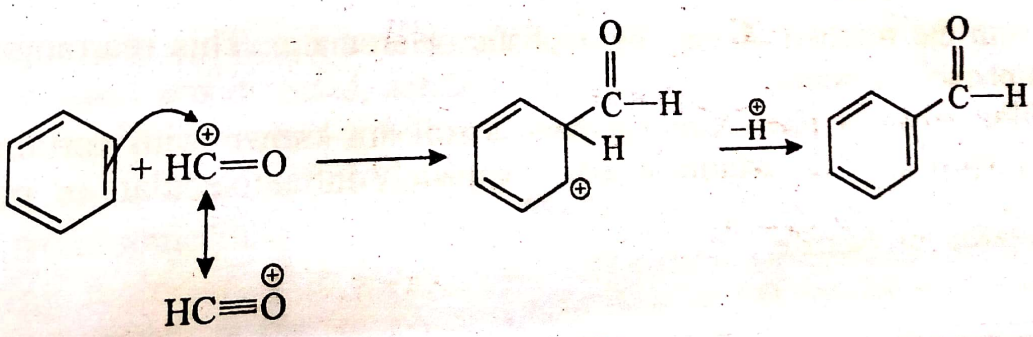

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oxychloride to give dihydroisoquinolines, which can be aromatized to isoquinolines.

7. Diazonium Coupling

Aromatic diazonium salts react with phenols, naphthols, and aromatic amines to form highly coloured azo compounds (azo dyes). This reaction is known as coupling reaction. The azo compounds are of great importance as dyes; about half of the dyes in industrial use today are azo dyes.

$$Ar\overset{\oplus}{N}_2 + Ar'H \longrightarrow \underset{\text{Azo compound}}{Ar—N=N—Ar'} + H$$

The aromatic ring (Ar′H) undergoing attack by the diazonium ion electrophile must contain a powerful electron-releasing group such as OH, NR_2, NHR or NH_2. The coupling usually occurs *para* to the activating group, if the *para* position is already occupied, it takes place at *ortho* position. This is presumably because of the size of the attacking diazonium ion.

Phenols couple fastest in mildly alkaline solutions because phenoxide ion is much more reactive than the un-ionised phenol in aromatic electrophilic substitution, and phenols themselves are not active enough for the coupling reaction. For amines the solution may be mildly acidic or neutral. If the acidity is too high, the reaction does not occur because the concentration of free amine becomes too small, and most of the amine is in the form of amine salt in which the ring is deactivated due to the – I effect of the ammonium ion group. In mildly acidic solution the concentration of the attacking electrophile $Ar—\overset{\oplus}{N}_2$ is high. However, neither phenols nor amines react in strongly alkaline solution because the diazonium ion is converted into a diazo hydroxide Ar—N=N—OH and diazoate

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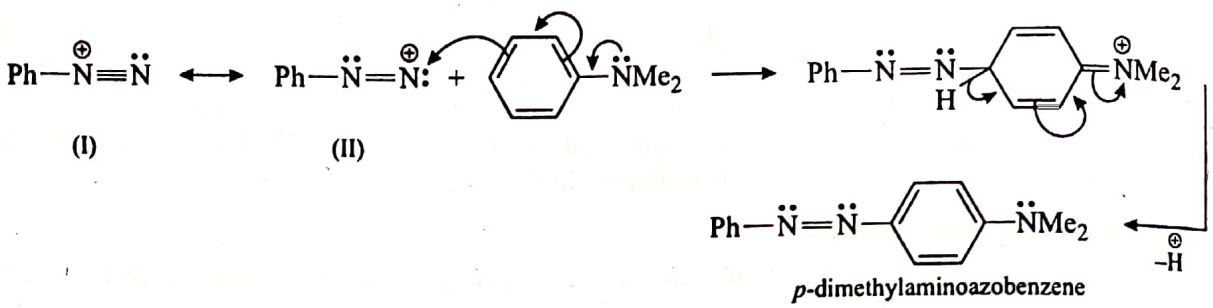
$Ar—N=N—\overset{\ominus}{O}\overset{\oplus}{Na}$ which ~~do not~~ couple.

$$Ar—\overset{\oplus}{N}\equiv N \xrightleftharpoons[\oplus H]{NaOH} Ar—N=N—OH \xrightleftharpoons[\oplus H]{NaOH} Ar—N=N—\overset{\ominus}{O}\overset{\oplus}{Na}$$

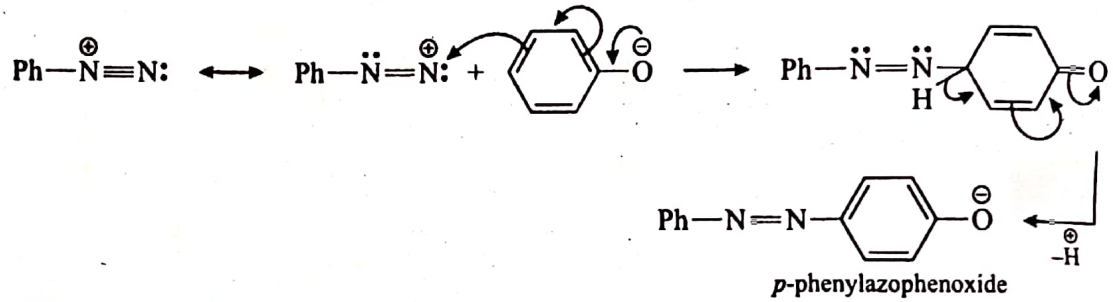
Couples — Does not couple — Does not couple



(I) (II)

p-dimethylaminoazobenzene

A detailed study of the coupling reaction has shown that it involves electrophilic substitution, the

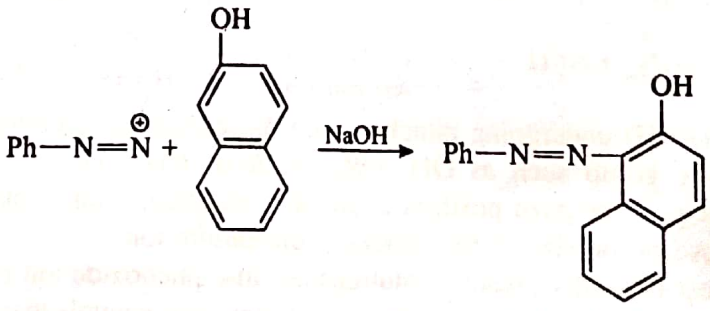


p-phenylazophenoxide

electrophile being the diazonium cation and the substrate being the free amine or the phenoxide ion :

The coupling of phenoxide ion similarly occurs as follows :

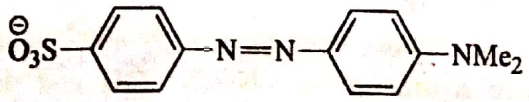
Since II is the reactive resonating structure, any factor that increases its contribution will increase the reactivity of that diazonium cation. Electrron-withdrawing group would favour II and electron-releasing group would favour I. This has been found to be so in practice, *e.g.*, *p*-nitrobenzenediazonium cation is more than 10,000 times as reactive as the *p*-methoxybenzenediazonium cation under the same conditions. The 2,4,6-trinitrobenzenediazonium cation is so reactive that it couples with certain hydrocarbons, *e.g.*, mesitylene.



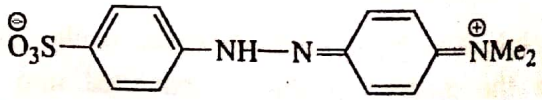
1-phenylazo-2-naphthol
orange-red color (azo dye)

2-Naphthol in alkaline solution couples with diazonium salts to give 1-phenylazo-2-naphthol, this reaction is used to test primary aromatic amines :

Methyl orange (*Helianthin*) is prepared by coupling diazotised sulphanilic acid with



Orange



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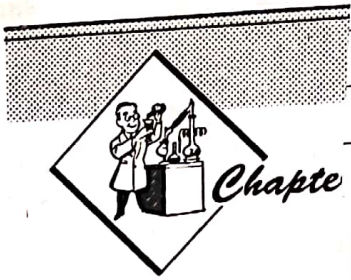

8 FREE RADICAL REACTIONS

8.0 FREE RADICAL REACTIONS

A *free radical* (or *radical*) may be defined as a species that contains one or more unpaired electrons.

Due to the presence of unpaired electron(s) free radicals are paramagnetic.

Types of free radical reactions : Free radical reactions are of two types, *i.e.*, propagation reactions and termination reactions. Involving these reactions, free radicals undergo most of the general types of reactions such as substitution, addition, rearrangement, oxidation and reduction.

Propagation reactions : These lead to other radicals, which themselves react further. There are four main propagation reactions, of which the first two are most common :

1. Abstraction of another atom or group, usually a hydrogen atom :

$$R^{\bullet} + R'\text{—H} \longrightarrow RH + R''^{\bullet}$$

2. Addition to multiple bonds :

$$R^{\bullet} + \text{—C=C—} \longrightarrow R\text{—C—C}^{\bullet}$$

3. Decomposition :

$$R\text{—C(=O)—O}^{\bullet} \xrightarrow{\beta\text{-Cleavage}} R^{\bullet} + CO_2$$

$$CH_3\text{—}CH_2\text{—}CH_2\text{—}\dot{C}H_2 \xrightarrow{\beta\text{-Cleavage}} CH_3\text{—}\dot{C}H_2 + CH_2\text{=}CH_2$$

4. Rearrangement :

$$R\text{—C(R)—}\dot{C}H_2 \longrightarrow R\text{—}\dot{C}\text{(R)—}CH_2\text{—}R$$

Termination reactions : These give stable products. The most common termination reactions are simple combinations of similar or different radicals :

$$R^{\bullet} + R''^{\bullet} \longrightarrow R\text{—}R'$$

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Another termination process is disproportionation.

$$2CH_3—\dot{C}H_2 \longrightarrow CH_3—CH_3 + CH_2=CH_2$$

In disproportionation reaction an alkane and an alkene are produced from a pair of radicals. A hydrogen atom of one radical is abstracted by another radical.

8.1 FREE RADICAL MECHANISM

Mechanism of free radical reactions generally involves three main steps, *i.e.*, *initiation*, *propagation* and *termination*. Each of these steps may consist of two or more steps.

Initiation step : In the initiation step(s) free radicals required for a reaction are generated *in situ* by irradiation or heating of the reagent or by carrying out the reaction in the presence of an *initiator* like peroxides, (*e.g.*, benzoyl peroxide). This process is always endothermic. For example, generation of bromine free radical from HBr :

(i) $Ph—\overset{O}{\overset{\|}{C}}—O—O—\overset{O}{\overset{\|}{C}}—Ph \longrightarrow 2Ph—\overset{O}{\overset{\|}{C}}—O^{\bullet}$ (ii) $Ph—\overset{O}{\overset{\|}{C}}—O^{\bullet} \longrightarrow Ph^{\bullet} + CO_2$

(iii) $Ph^{\bullet} + H—Br \longrightarrow PhH + Br^{\bullet}$

Propagation Step : When a radical reacts with a molecule (which has an even number of electrons), a new radical is generated. This type of step is called propagation because the newly formed radical can now react with another molecule and produce another radical, and so on, until two radicals combine and terminate the sequence. Such reactions where there are hundreds or thousands of propagation steps between an initiation and termination are called *chain reactions*. Free radical chain reactions work best when all propagation steps are exothermic. An endothermic step corresponds to a slow and reversible reaction that breaks the chain.

$$Br^{\bullet} + CH_2=CH—CH_3 \longrightarrow BrCH_2—\dot{C}H—CH_3$$

$$BrCH_2—\dot{C}H—CH_3 + H—Br \longrightarrow BrCH_2—CH_2—CH_3 + Br^{\bullet}$$

Termination Step : In this step free radicals are destroyed by coupling of two same or different radicals or by disproportionation :

$$R^{\bullet} + R''^{\bullet} \longrightarrow R—R'$$

$$2CH_3—\dot{C}H_2 \longrightarrow CH_3—CH_3 + CH_2=CH_2$$

Inhibitors : A chain reaction of free radicals may also be terminated by adding free radical inhibitors, *e.g.*, benzoquinone, phenols, amines, thiols, nitric oxide, oxygen, etc. Oxygen acts as free radical inhibitor by forming a peroxide free radical which is much less reactive, thus it breaks the chain.

$$R^{\bullet} + O_2 \longrightarrow R—O—O^{\bullet}$$

An inhibitor may be defined as a substance that slows down or stops a free radical reaction even though present in small amount.

General characteristics of free radical reactions :

1. Reactions are similar whether they are occurring in the vapour or liquid phase.
2. They are unaffected by the presence of acids or bases or by changes in the polarity of solvents.
3. They are initiated or accelerated by typical free radical sources such as peroxides, or by light.

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4. Their rates are decreased or the reactions are stopped by substances that scavenge free radicals, *e.g.*, nitric oxide, benzoquinone, or O_2. These substances are called *inhibitors*.

8.2 FREE RADICAL SUBSTITUTION MECHANISMS

Halogenation at an alkyl carbon

Alkanes can be chlorinated or brominated on reaction with chlorine or bromine in the presence of visible or *uv* light, or at high temperatures (250–400°C). For example :

$$R\text{—H} + Cl_2 \xrightarrow[\text{or } 250\text{–}400^\circ C]{h\nu} R\text{—Cl} + HCl$$

The reaction can also be applied to alkyl chains containing many functional groups. The chlorination reaction is not useful for preparative purposes because every alkyl carbon in the molecule is chlorinated as well as *di-* and polychloro compounds are formed. The bromination is much more selective than chlorination. It is possible to brominate tertiary and benzylic positions selectively. It should be remembered that *the greater the reactivity of a species, the less is the selectivity.*

It should be noted that fluorine reacts too violently involving rupture of C—C bonds, whereas iodine reacts too slowly and reversibly to be of any practical interest.

Mechanism : The halogenation at an alkyl carbon is a free radical chain reaction and proceeds through the following mechanism:

Initiation step

$$X_2 \xrightarrow[\text{or } 250\text{–}400^\circ C]{h\nu} 2X^\bullet$$

Propagation steps

$$R\text{—H} + X^\bullet \longrightarrow R^\bullet + HX$$

$$R^\bullet + X_2 \longrightarrow R\text{—}X + X^\bullet$$

Termination steps

$$R^\bullet + X^\bullet \longrightarrow R\text{—}X$$

$$X^\bullet + X^\bullet \longrightarrow X_2$$

$$R^\bullet + R^\bullet \longrightarrow R\text{—}R$$

The following is the decreasing order of reactivity of halogens :

$$F_2 > Cl_2 > Br_2 > I_2$$

The most important single factor causing the order of halogen reactivity is the decreasing strength of the H—*X* bond which is in the order :

$$H\text{—}F > H\text{—}Cl > H\text{—}Br > H\text{—}I$$

This is because with increasing H—*X* bond strength the propagation step :

$$R\text{—H} + X^\bullet \longrightarrow R^\bullet + HX$$

is favoured, which is the rate-determing step at least in the case of methane.

The following is the decreasing order of the ease of abstraction of different kinds of hydrogens : tertiary H > secondary H > primary H > methane H. This order is easily understandable in view of the relative stabilities of the free radicals formed after the abstraction of hydrogen.

Stereochemistry of Radical Substitution : The alkyl radical having planar structure is attacked from both the faces with equal ease to form racemic modifacion. For example :

$$CH_3\text{—}CH_2\text{—}CH_2\text{—}CH_3 + Br^\bullet \longrightarrow \underset{\substack{\text{Radical carbon has}\\ \text{planar structure}}}{CH_3\text{—}CH_2\text{—}\overset{\bullet}{C}H\text{—}CH_3} + HBr$$

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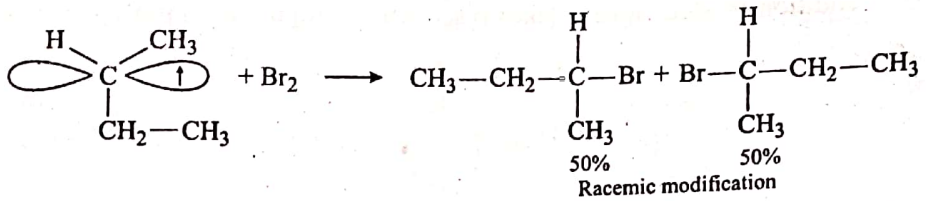
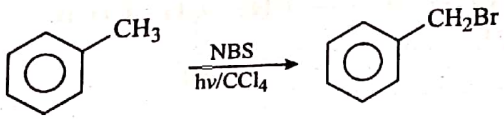


Allylic Halogenation : Alkenes can be halogenated in the allylic position by a number of reagents such as *N*-bromosuccinimide (NBS), N-chlorosuccinimide (NCS), *t*-butyl hypochlorite, etc., of these, NBS is the most common. When NBS is used, the reaction is known as ***Wohl-Ziegler reaction***. Using NBS rather than bromine for allylic bromination solves the problem of formation of the undesired addition product of alkene with bromine.

The reaction of NBS is highly regioselective and takes place at the allylic position. NBS is also a highly regioselective brominating agent at positions α to an aromatic ring (benzylic position), to a C≡C triple bond, to a carbonyl group. When both double and triple bonds are in the same molecule, the preferred position is α to the triple bond.

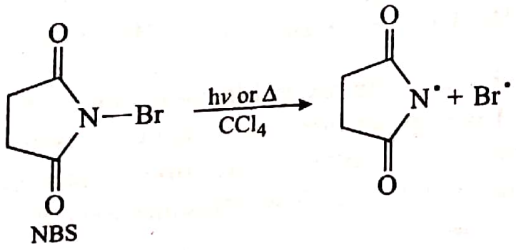
Examples :

(i) $CH_3—CH=CH_2 \xrightarrow[h\nu/CCl_4]{NBS} Br—CH_2—CH=CH_2$

(ii) 

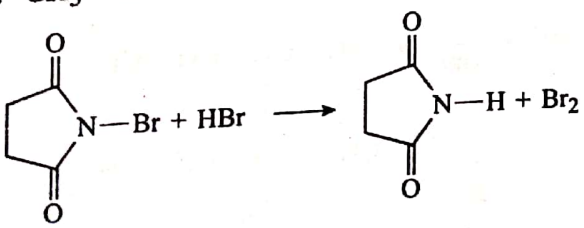
(iii) $HC\equiv C—CH_3 \xrightarrow[h\nu/CCl_4]{NBS} HC\equiv C—CH_2Br$

The reaction of NBS is carried out in nonpolar solvent, most often CCl_4 is used. NBS is only slightly soluble in CCl_4, this ensures the low concentration of bromine necessary for the success of this reaction. The reaction is catalysed by peroxides, heat or light.

Step 1. 

Mechanism :

Step 2. $CH_3—CH=CH_2 + Br^{\bullet} \longrightarrow \dot{C}H_2—CH=CH_2 + HBr$

Step 3. 

Step 4. $\dot{C}H_2—CH=CH_2 + Br_2 \longrightarrow Br—CH_2—CH=CH_2 + Br^{\bullet}$

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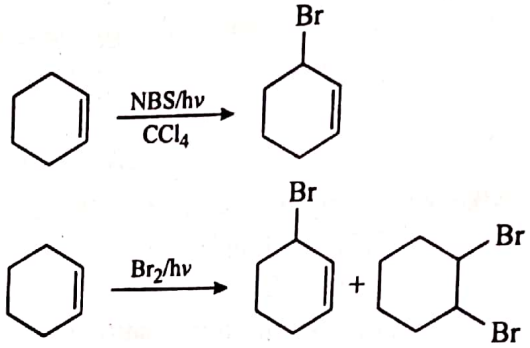
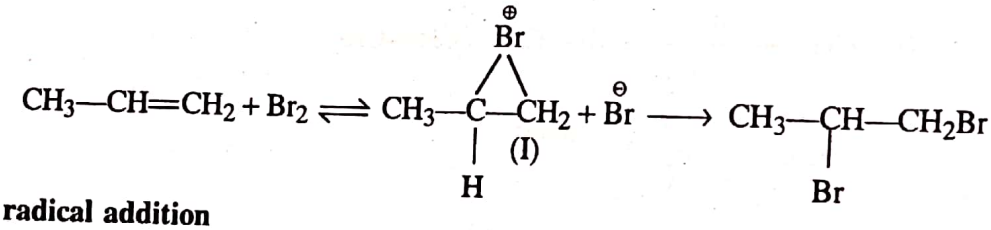
Formation of addition product always takes place when a high concentration of bromine is used.



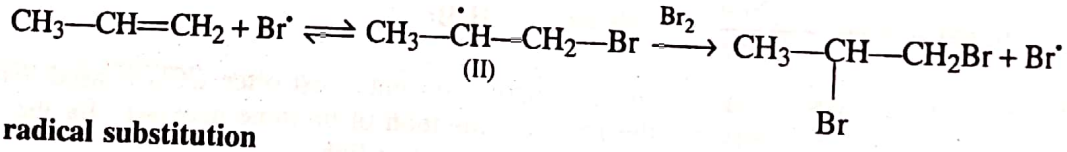
The function of NBS is to provide a low, constant concentration of bromine and to use up the HBr formed in **step 2**.

Why is an ionic or a free radical addition to the double bond not observed with NBS if bromine is the reacting species? This is because the concentration of bromine in the reaction mixture is too low.

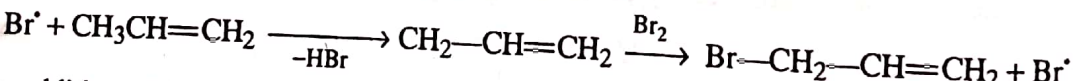
Ionic addition :



Free radical addition



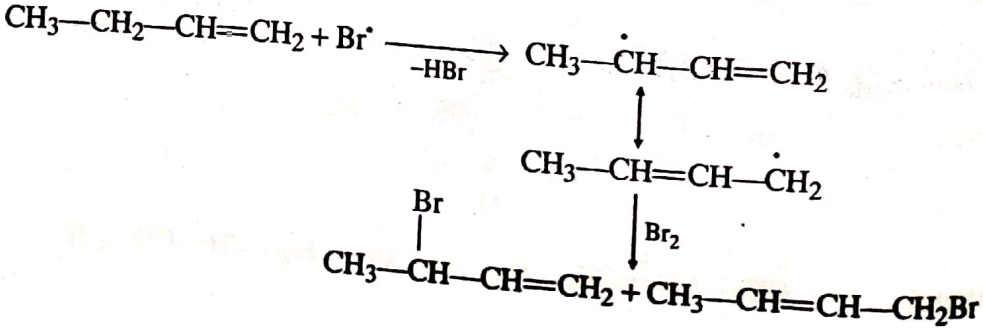
Free radical substitution



The addition of bromine to the double bond involves the reversible formation of the bromonium ion I or the free radical II. If the concentration of the proper bromine-containing species is too low, the intermediates I and II revert to the initial species and the allylic substitution competes successfully. This explanation is confirmed by running the reaction with very low concentrations of Br_2, in which case allylic substitution rather than addition takes place.

In cases where the allylic intermediate is unsymmetrical, allylic reaerrangement occurs to give a mixture of both possible products.

For example :



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When a double bond has two different allylic positions, *e.g.*, $CH_3—CH=CH—CH_2CH_3$, a secondary position is substituted more readily than a primary. The relative reactivity of tertiary hydrogen is not clear. It is possible to brominate both sides of the double bond. Because of the electron-withdrawing nature of bromine, the second bromine substitutes on the other side of the double bond rather than α to the first bromine, for example :

$$CH_3—CH=CH—\underset{\displaystyle Br}{\underset{|}{CH}}—CH_3 \xrightarrow[CCl_4/\Delta]{NBS} Br—CH_2—CH=CH—\underset{\displaystyle Br}{\underset{|}{CH}}—CH_3$$

Free radical mechanism at an aromatic substrate : Hey (1934) reported that the thermal decomposition of diazonium salts in aromatic solvents results in the arylation of the aromatic rings. He explained these results by the following mechanism involving the direct displacement of a hydrogen atom in the aromatic solvent molecule by the aryl radical, *i.e.*, the abstraction of an entire aryl group of the solvent molecule by the aryl radical.

$$Ar—N=NX \longrightarrow Ar^{\bullet} + N_2 + X^{\bullet}$$

$$Ar^{\bullet} + Ph—H \longrightarrow Ar—Ph + H^{\bullet}$$

[X = Cl, OAc, OH]

Similar results are obtained from the aryl radicals generated from other sources such as the decomposition of benzoyl peroxide in aromatic solvents.

$$Ph—\overset{\displaystyle O}{\overset{\|}{C}}—O—O—\overset{\displaystyle O}{\overset{\|}{C}}—Ph \longrightarrow 2Ph—\overset{\displaystyle O}{\overset{\|}{C}}—O^{\bullet} \longrightarrow 2Ph^{\bullet} + 2CO_2$$

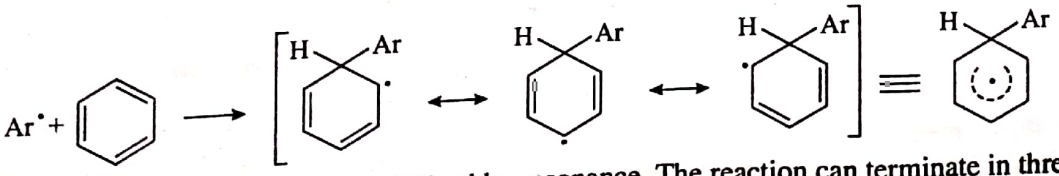
$$Ph^{\bullet} + Ph—H \longrightarrow Ph—Ph + H^{\bullet}$$

The above direct displacement mechanism was discarded because :

1. It involves the formation of a C—C bond at the expense of a relatively stronger C—H bond (*i.e.*, abstraction of an entire aryl group) which requires a very high activation energy, thus, actually this is not the case.
2. It does not explain the formation of products I and II.

The following two-step mechanism which is exothermic and also explains the formation of products I and II was proposed. This is similar to the mechanism of aromatic electrophilic and nucleophilic substitutions.

$$Ar—\overset{\displaystyle O}{\overset{\|}{C}}—O—O—\overset{\displaystyle O}{\overset{\|}{C}}—Ar \longrightarrow 2Ar—\overset{\displaystyle O}{\overset{\|}{C}}—O^{\bullet} \longrightarrow 2Ar^{\bullet} + 2CO_2$$



The intermediate free radical is stabilised by resonance. The reaction can terminate in three ways:

(i) By simple coupling :

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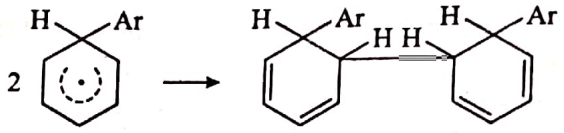
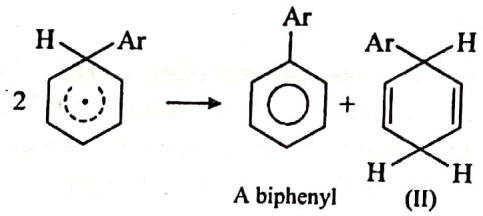


(I)

A partially hydrogenated quaterphenyl

The coupling need not be *ortho-ortho*, other isomer can also be formed.

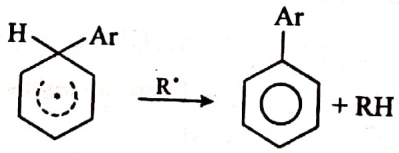
(ii) Disproportionation :



A biphenyl (II)

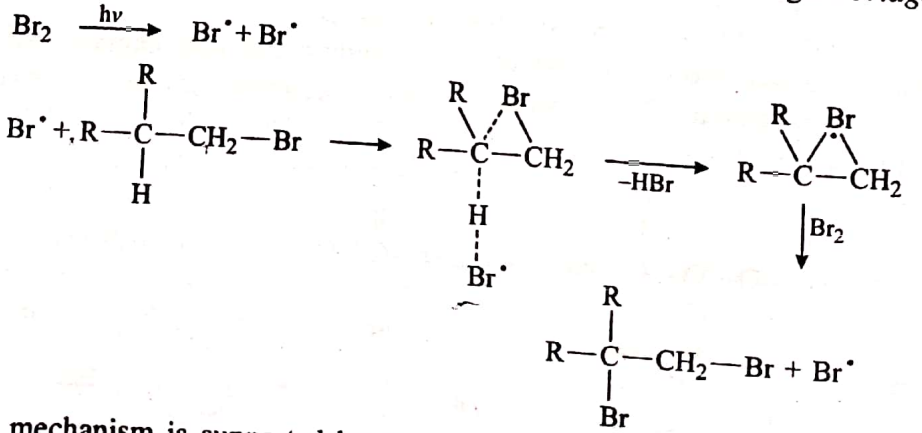
Under the reaction conditions dihydrobiphenyls like II are oxidised to the corresponding biphenyls.

(iii) By abstraction of hydrogen, if a radical $R^{\bullet}$ is present in the system :



8.3 NEIGHBOURING GROUP ASSISTANCE IN FREE RADICAL REACTIONS

In certain cases it has been shown that free radical reactions are accelerated by the presence of neighbouring groups. For example, bromination of alkyl bromides gave 84 to 94% substitution at the carbon adjacent to the bromine already present in the molecule. This is surprising because positions close to a $-I$ group such as bromine should actually be deactivated by its electron-withdrawing effect. This unusual regioselectivity is explained by the following mechanism in which the abstraction of hydrogen is assisted by a neighbouring group and the reaction proceeds through a *bridged free radical.*



The above mechanism is supported by the fact that as expected it proceeds with retention of configuration. Thus photolytic bromination of optically active 1-bromo-2-methylbutane gives 1,2-dibromo-2-methylbutane with retention of configuration.

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8.4 REACTIVITY

Reactivity for Aliphatic Substrates

It is the abstraction step that determines which product will be formed in a chain reaction. A free radical almost always abstracts a univalent (hydrogen or halogen) and never a tetra- or tercovalent atom, and seldom a divalent one. For example, a reaction between a chlorine free radical and ethane gives an ethyl radical, not a hydrogen free radical :

$$CH_3—CH_3 + Cl^{\bullet} \rightarrow H—Cl + CH_3\dot{C}H_2 \quad \Delta H = -3 \text{ kcal/mole}$$

$$CH_3—CH_3 + Cl^{\bullet} \not\rightarrow CH_3CH_2—Cl + \dot{H} \quad \Delta H = +18 \text{ kcal/mole}$$

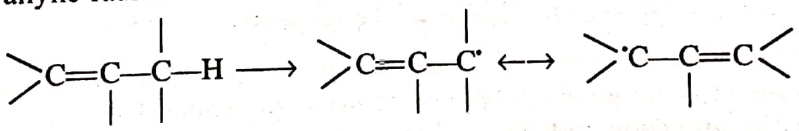
The main reason for this is steric. A univalent atom is much more exposed to attack by the incoming radical than an atom with a higher valency. Another reason is that in many cases abstraction of a univalent atom is energetically more favoured.

In the case of alkanes, the following is the decreasing order of the ease of abstraction of different kinds of hydrogens :

tertiary H > secondary H > primary H > methane H

This is according to the relative stabilities of the free radicals formed after the abstraction of hydrogen.

In the case of alkenes vinylic hydrogens are never abstracted, and the abstraction of allylic hydrogens is greatly preferred to other positions of the molecule. This is because of the resonance stabilisation of the allylic radical :

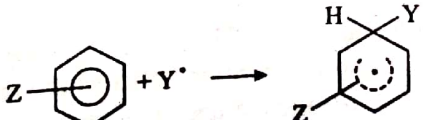


Allylic rearrangements are common in these cases.

In the case of alkyl chains of aromatic rings the preferential position of attack on a side chain is usually the position α to the ring. Aromatic hydrogens are seldom abstracted if there are aliphatic hydrogens present.

In the case of compounds containing electron-withdrawing substituents, *e.g.*, $Z—CH_2CH_3$ ($Z = COOH$, $COCl$, $COOR$, SO_2Cl, or CX_3) the β position is attacked predominantly or exclusively in free radical halogenations. This is because electron-withdrawing groups highly deactivate adjacent (α) positions. Compounds like acetic acid and acetyl chloride are not attacked at all. This is because halogen atoms are electrophilic radicals and look for positions of high electron density. Hydrogens on carbon atoms next to the electron-withdrawing groups have low electron densities, therefore, the attack is avoided at this position. The radicals that are not electrophilic do not show this behaviour, *e.g.*, the methyl radical does not avoid the attack at the α position. Some radicals, *e.g.*, *t*-butyl, benzyl, cyclopropyl and phenyl are nucleophilic and tend to abstract electron-poor hydrogens.

Reactivity in Aromatic Substrates : Free radical substitution at an aromatic carbon seldom takes place by a mechanism in which a ring hydrogen is abstracted to give an aryl radical. Usually, the mechanism is similar to that of aromatic electrophilic and nucleophilic substitutions.



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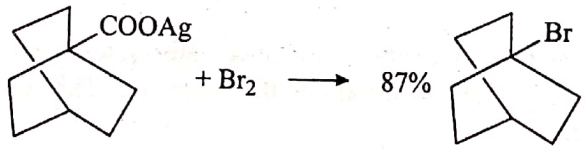
The following generalisations have been made regarding the reactivity in aromatic substrates :

1. All substituents increase reactivity at *ortho* and *para* positions as compared to that of benzene. There is no great difference between electron-donating and electron-withdrawing groups. This is because radicals are neutral species and are not influenced by the polar properties of the substrate to any significant extent. Furthermore, it has been shown that both electron-donating and electron-withdrawing groups stabilise a free radical.
2. Reactivity at *meta* positions is almost equal to that of benzene. This fact, coupled with preceding one, means that all substituents are activating and *ortho-para* directing; none are deactivating or mainly *meta* directing.
3. Reactivity at *ortho* positions is greater than at *para* positions, except where a large group decreases *ortho* reactivity due to steric reasons.
4. Electron-withdrawing groups exert a greater *ortho-para* directing and activating effect than electron-donating groups.
5. Substituents have a much smaller effect than in electrophilic or nucleophilic substitution.
6. Although hydrogen is the leaving group in most free radical aromatic substitutions, *ipso* attack and *ipso* substitution (*e.g.*, with Br, NO_2, or CH_3CO as the leaving group) have been found in certain cases.

Reactivity at a Bridgehead : Many free radical reactions have been observed at bridgehead carbons. For example, in the following reaction a free radical is formed at the bridgehead carbon.



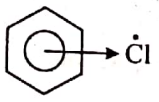
(For mechanism see Section 8.10)

This demonstrates that the free radical need not be planar. Although bridgehead free radical substitution is possible, it is not preferred because of the strain involved.

Reactivity in the attacking radicals : The greater the reactivity of a species, the less is the selectivity. The bromine atom is so selective that when only primary hydrogen are available, as in neopentane or *t*-butylbenzene, the reaction is slow or nonexistent. Isobutane can be selectively brominated to give *t*-butyl bromide, and toluene reacts with bromine instantly. Other alkylbenzenes, *e.g.*, ethylbenzene and cumene are brominated exclusively at the α position emphasizing the selectivity of bromine free radical.

Some radicals, *e.g.*, triphenylmethyl, are so unreactive that they abstract hydrogens very slowly. As mentioned earlier, some free radicals, *e.g.*, chloro, are electrophilic and some, *e.g.*, *t*-butyl are nucleophilic. However, the predominant character of a free radical is neutral, whether it has slight electrophilic or nucleophilic tendency.

The effect of solvent on reactivity : Unlike ionic substitutions, the solvent usually has little effect on free radical substitutions. Free radical reactions in solution are quite similar in character to those in the gas phase, where there is no solvent. However, in certain cases the solvent can make an appreciable difference. For example, chlorination of 2,3-dimethylbutane in aliphatic solvents gave



about 60% $(CH_3)_2CHCH(CH_3)CH_2Cl$ and 40% $(CH_3)_2CHCCl(CH_3)_2$, while in aromatic solvents the ratio became 10 : 90. This is due to complex formation between the aromatic solvent and the chlorine free radical which makes the chlorine less reactive and thus, more selective.

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